

REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)

In re Application of

PROCESSED BY

JUN 17 1998

FII

Application Number		Filed
08 /359,945		12-20-94
Group Art Unit	Examiner	

Assistant Commissioner for Patents
Washington, DC 20231Paper No. 7023

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE)

(A) referred to in United States Patent Number 5,750,376, column Face

(B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. _____, filed _____ on page _____ of paper number _____

(C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. _____, filed _____, or

(D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

Please direct any correspondence concerning this request to the following address:

Mike Surles

Signature

Mike Surles

Typed or printed name

6-19-98

Date

FOR PTO USE ONLY

Approved by: PL

(initials)

Unit: File Information



#23

United States Patent [19]

Weiss et al.

[11] Patent Number: 5,750,376

[45] Date of Patent: May 12, 1998

[54] IN VITRO GROWTH AND PROLIFERATION OF GENETICALLY MODIFIED MULTIPOTENT NEURAL STEM CELLS AND THEIR PROGENY

93/09802 5/1993 WIPO
94/03199 2/1994 WIPO

[75] Inventors: **Samuel Weiss**; **Brent Reynolds**, both of Alberta, Canada; **Joseph P. Hammang**; **E. Edward Baetge**, both of Barrington, R.I.

[73] Assignee: **NeuroSpheres Holdings Ltd.**, Calgary, Canada

[21] Appl. No.: 483,122

[22] Filed: Jun. 7, 1995

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 270,412, Jul. 5, 1994, abandoned, Ser. No. 385,404, Feb. 7, 1995, abandoned, Ser. No. 359,945, Dec. 20, 1994, abandoned, Ser. No. 376,062, Jan. 20, 1995, abandoned, Ser. No. 149,508, Nov. 9, 1993, abandoned, Ser. No. 311,099, Sep. 23, 1994, abandoned, and Ser. No. 338,730, Nov. 14, 1994, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, said Ser. No. 385,404, Feb. 7, 1995, abandoned, is a continuation of Ser. No. 961,813, Oct. 16, 1992, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, said Ser. No. 359,345, Dec. 20, 1994, abandoned, is a continuation of Ser. No. 221,655, Apr. 1, 1994, abandoned, which is a continuation of Ser. No. 967,622, Oct. 28, 1992, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, said Ser. No. 376,062, Jan. 20, 1995, abandoned, is a continuation of Ser. No. 10,829, Jan. 29, 1993, abandoned, which is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned, said Ser. No. 270,412, Jul. 5, 1994, abandoned, Ser. No. 149,508, Nov. 9, 1993, abandoned, and Ser. No. 311,099, Sep. 23, 1994, abandoned, each is a continuation-in-part of Ser. No. 726,812, Jul. 8, 1991, abandoned.

[51] Int. Cl. ⁶ C12N 5/00; C12N 5/08; C12N 5/10; C12P 1/00

[52] U.S. Cl. 435/69.52; 435/69.1; 435/172.3; 435/325; 435/368; 435/377; 435/384; 435/392; 435/395

[58] Field of Search 435/240.2, 172.3, 435/69.1, 69.52, 325, 368, 377, 384, 392, 395

[56] References Cited

U.S. PATENT DOCUMENTS

4,753,635 6/1988 Sagen et al. 604/49
4,980,174 12/1990 Sagen et al. 424/563
5,082,670 1/1992 Gage 424/520
5,175,103 12/1992 Lee et al. 435/172.3
5,411,883 5/1995 Boss et al. 435/240.2
5,612,211 3/1997 Wilson et al. 435/378

FOREIGN PATENT DOCUMENTS

0 233 838 8/1987 European Pat. Off.
89/03872 5/1989 WIPO
90/06757 6/1990 WIPO
91/02003 2/1991 WIPO
91/09936 7/1991 WIPO
91/17242 11/1991 WIPO
93/01275 1/1993 WIPO

OTHER PUBLICATIONS

Almazan et al., "Epidermal Growth Factor and Bovine Growth Hormone Stimulate Differentiation and Myelination of Brain Cell Aggregates in Culture," *Developmental Brain Research*, 21:257-264 (1985).

Anchan et al., "Trophic Factors Influence Proliferation of Germinal Neuroepithelial Cells of the Retina," *J. Cell Biol.*, 109:58a, Abstract No. 308 (1989).

Anchan et al., "EGF and TGF- α Stimulate Retinal Neuroepithelial Cell Proliferation in Vitro," *Neuron*, 6(6):923-936 (1991).

Bayer et al., "Neuron production in the Hippocampus and olfactory bulb of the adult rat Brain: addition or replacement?", *Annals NY Acad. Sci.* 457:163-172 (1985).

Björklund et al., "Neural Grafting in Animal Models of Neurodegenerative Diseases," *Ann. New York Acad. Sci.*, 457:53-81 (1985).

Bouvier et al., "Basic Fibroblast Growth Factor (bFGF) Promotes the Survival and Proliferation of Mesencephalic Neuronal Precursors in Vitro," *Society for Neuroscience Abstracts*, vol. 18, Abstract No.: 403.7 (1992).

Boyles et al., "Accumulation of Apolipoproteins in the Regenerating and Remyelinating Mammalian Peripheral Nerve," *J. Biol. Chem.*, 265(29):17805-17815 (1990).

Calof et al., "Analysis of Neurogenesis in a Mammalian Neuroepithelium: Proliferation and Differentiation of an Olfactory Neuron Precursor in Vitro," *Neuron*, 3:115-127 (1989).

(List continued on next page.)

Primary Examiner—George C. Elliott

Assistant Examiner—Johnny F. Railey, II

Attorney, Agent, or Firm—Flehr Hohbach Test Albritton & Herbert; David J. Brezner; Jan P. Brunelle

[57] ABSTRACT

A method for producing genetically modified neural cells comprises culturing cells derived from embryonic, juvenile, or adult mammalian neural tissue with one or more growth factors that induce multipotent neural stem cells to proliferate and produce multipotent neural stem cell progeny which include more daughter multipotent neural stem cells and undifferentiated progeny that are capable of differentiating into neurons, astrocytes, and oligodendrocytes. The proliferating neural cells can be transfected with exogenous DNA to produce genetically modified neural stem cell progeny. The genetic modification can be for the production of biologically useful proteins such as growth factor products, growth factor receptors, neurotransmitters, neurotransmitter receptors, neuropeptides and neurotransmitter synthesizing genes. The multipotent neural stem cell progeny can be continuously passaged and proliferation reinitiated in the presence of growth factors to result in an unlimited supply of neural cells for transplantation and other purposes. Culture conditions can be provided that induce the genetically modified multipotent neural stem cell progeny to differentiate into neurons, astrocytes, and oligodendrocytes in vitro.